### \* \*TENT COOPERATION TRE Y

## From the INTERNATIONAL BUREAU PCT Commissioner **NOTIFICATION OF ELECTION** US Department of Commerce United States Patent and Trademark (PCT Rule 61.2) Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 **ETATS-UNIS D'AMERIQUE** Date of mailing (day/month/year) in its capacity as elected Office 17 July 2001 (17.07.01) International application No. Applicant's or agent's file reference PCT/US00/26797 117-321 International filing date (day/month/year) Priority date (day/month/year) 29 September 2000 (29.09.00) 01 October 1999 (01.10.99) **Applicant** TAN, Yin, Hwee et al 1. The designated Office is hereby notified of its election made: X in the demand filed with the International Preliminary Examining Authority on: 12 April 2001 (12.04.01) in a notice effecting later election filed with the International Bureau on: 2. The election was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

H. Zhou

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

## \*\*TENT COOPERATION TRE. \* /

### From the INTERNATIONAL BUREAU

PCT	То:
NOTIFICATION OF ELECTION  (PCT Rule 61.2)	Commissioner US Department of Commerce United States Patent and Trademark Office, PCT 2011 South Clark Place Room CP2/5C24 Arlington, VA 22202 ETATS-UNIS D'AMERIQUE
Date of mailing (day/month/year) 29 August 2001 (29.08.01)	in its capacity as elected Office
International application No. PCT/US00/26797	Applicant's or agent's file reference 117-321
International filing date (day/month/year) 29 September 2000 (29.09.00)	Priority date (day/month/year) 01 October 1999 (01.10.99)
Applicant TAN, Yin, Hwee et al	
1. The designated Office is hereby notified of its election made    X   in the demand filed with the International Preliminary   12 April 2001 (1)	Examining Authority on: 12.04.01) ational Bureau on:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

Farid ABBOU

Facsimile No.: (41-22) 740.14.35 Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY



1 REC'D 2 7 FEB 2002

WPO

### PCT INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

	······································	
Applicant's or agent's file reference N.77877A CMK	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.	International filing date (day/monti	//year) Priority date (day/month/year)
PCT/US00/26797	29/09/2000	01/10/1999
International Patent Classification (IPC) or not A61K31/00  Applicant INSTITUTE OF MOLECULAR AND  1. This international preliminary exammand is transmitted to the applicant according to the according to	CELL BIOLOGY et al.  nination report has been prepared according to Article 36.	by this International Preliminary Examining Authority
been amended and are the bas	sis for this report and/or sheets on the Administrative Instruction	e description, claims and/or drawings which have ontaining rectifications made before this Authority ons under the PCT).
IV	pinion with regard to novelty, involved to novelty, involved to reder Article 35(2) with regard to represent supporting such statement and the redering such statement are retained to retain the redering such statement are retained to retain the redering such statement are retained to retain the redering	entive step and industrial applicability novelty, inventive step or industrial applicability;
VIII   Certain observations or	n the international application	-
Date of submission of the demand	Date of c	ompletion of this report
12/04/2001	25.02.20	02
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 Fax: +49 89 2399 - 4465	Kling, I	e No. +49 89 2399 8471



I. Bas	is of t	he re	p nt
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1.	the an	e receiving Office in	nents of the international application (Replacement sheets which have been furnished to response to an invitation under Article 14 are referred to in this report as "originally filed" of this report since they do not contain amendments (Rules 70.16 and 70.17)):
•	1-3	38	as originally filed
	Cla	aims, No <del>.:</del>	
	1-3	34	as originally filed
2.			juage, all the elements marked above were available or furnished to this Authority in the nternational application was filed, unless otherwise indicated under this item.
	The	ese elements were a	available or furnished to this Authority in the following language: , which is:
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pu	blication of the international application (under Rule 48.3(b)).
		the language of a f 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule
3.			leotide and/or amino acid sequence disclosed in the international application, the y examination was carried out on the basis of the sequence listing:
		contained in the in	ternational application in written form.
		filed together with	the international application in computer readable form.
		furnished subsequ	ently to this Authority in written form.
		furnished subsequ	ently to this Authority in computer readable form.
			the subsequently furnished written sequence listing does not go beyond the disclosure in oplication as filed has been furnished.
		The statement that listing has been ful	the information recorded in computer readable form is identical to the written sequence nished.
4.	The	e amendments have	resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:
		the drawings,	sheets:
5.			en established as if (some of) the amendments had not been made, since they have been eyond the disclosure as filed (Rule 70.2(c)):



(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6.	Add	ditional observations, if n	ecessa	ry:	
III.	No	n-establishment of opir	nion wit	th regard	d to novelty, inventive step and industrial applicability
1.	obv	rious), or to be industriall	y applic	able hav	on appears to be novel, to involve an inventive step (to be non- ve not been examined in respect of:
	⋈	the entire international claims Nos. 1,15-25,29			
be	caus	se:			
		the said international ap not require an internation			e said claims Nos. relate to the following subject matter which does examination ( <i>specify</i> ):
		the description, claims of that no meaningful opin			dicate particular elements below) or said claims Nos. are so unclear med (specify):
		the claims, or said claim could be formed.	ns Nos.	are so ir	inadequately supported by the description that no meaningful opinion
	×	no international search	report h	as been	established for the said claims Nos. 1,15-25,29-34.
	and				ination cannot be carried out due to the failure of the nucleotide ly with the standard provided for in Annex C of the Administrative
		the written form has not	been fu	ırnished (	or does not comply with the standard.
		the computer readable f	orm has	s not bee	en furnished or does not comply with the standard.
		soned statement under			with regard to novelty, inventive step or industrial applicability; ch statement
1.	Stat	ement			
	Nov	elty (N)	Yes: No:	Claims Claims	•
	Inve	ntive step (IS)	Yes: No:	Claims Claims	· ·
•	Indu	strial applicability (IA)	Yes:	Claims	2-14 26-28

International application No. PCT/US00/26797

N	lo:	Cla	aims

2. Citations and explanations see separate sheet

### R Item III

# Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The claims relating to inventions in respect of which no international search report has been established need not to be the subject of an international preliminary examination. The Applicant is advised that the EPO policy when acting as an International Preliminary Authority is normally not to carry out a preliminary examination on matter which has not been searched.

### Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Claims 2 to 14 and 26 to 28 are concerned with the use of an inhibitor of dihydroorotate dehydrogenase of formula (I), (Ia) (II), (IIb), (I'), (III), (IV), (V), (VI), (VII) or (VIII) in the manufacture of a medicament for use in the treatment of an infection attributable to a virus of Flaviridae, Rhabdoviridae or Paramyxoviridae family and with a compound of formula (IIa) (claims 26 and 27) and a process for the manufacture of a compound of formula (IIa) (claim 28).

The documents cited in the International Search Report are:

- D1: US-A-4 680 299 (HESSON DAVID P) 14 July 1987 (1987-07-14) cited in the application
- D2: EP-A-0 601 191 (KYOWA HAKKO KOGYO KK) 15 June 1994 (1994-06-15)
- D3: PATENT ABSTRACTS OF JAPAN vol. 1998, no. 14, 31 December 1998 (1998-12-31) & JP 10 231289 A (KYOWA HAKKO KOGYO CO LTD), 2 September 1998 (1998-09-02) cited in the application
- D4: EP-A-0 721 942 (KYOWA HAKKO KOGYO KK) 17 July 1996 (1996-07-17)

D1 and D3 disclose compounds of Formula (I) and their use as tumour inhibiting agents or as immunosuppressant.

D2 and D4 disclose tetracyclic compounds close to the compounds of Formula (II) useful as immuno-suppressant.

## INTERNATIONAL PRESIMINARY **EXAMINATION REPORT - SEPARATE SHEET**

inventive step (Rule 65(1)(2) PCT).

International application No. PCT/US00/26797

The present application satisfies the criteria set forth in Articles 33(2) and 33(3) PCT because the subject-matter of Claims 2 to 14 and of claims 26 to 28 is new with respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT) and involves an

## (19) World Intellectual Property Organization International Bureau



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## (43) International Publication Date 12 April 2001 (12.04.2001)

**PCT** 

## (10) International Publication Number WO 01/24785 A2

- (51) International Patent Classification<sup>7</sup>: A61K 31/00, 31/47, 31/4709, 31/497, 31/473, 31/4184, 31/122, 31/196, C07D 215/52, A61P 31/14, A61K 38/21, 31/711, 31/343, 31/437 // (A61K 38/21, 31:00) (A61K 31/437, 31:00) (A61K 31/343, 31:00)
- (21) International Application Number: PCT/US00/26797
- (22) International Filing Date:

29 September 2000 (29.09.2000)

(25) Filing Language:

**English** 

(26) Publication Language:

English

(30) Priority Data:

60/157,017

1 October 1999 (01.10.1999) US

- (71) Applicant (for all designated States except US): INSTITUTE OF MOLECULAR AND CELL BIOLOGY [SG/SG]; 30 Medical Drive, Singapore 117609 (SG).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): TAN, Yin, Hwee [CA/SG]; 30 Medical Drive, Singapore 117609 (SG). DRISCOLL, John, Stanford [US/US]; 4 Infield Court South, Rockville, MD 20854 (US). MUI MUI, Sim [SG/SG]; 30 Medical Drive, Singapore 117609 (SG).

- (74) Agent: WILSON, Mary, J.; Nixon & Vanderhye PC, Suite 800, 1100 North Glebe Road, Arlington, VA 22201-4714 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, MIL, MR, NE, SN, TD, TG).

#### Published:

 Without international search report and to be republished upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

)

#### (54) Title: COMPOUNDS FOR THE TREATMENT OF VIRAL-MEDIATED DISEASES

PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification of (Form PCT/ISA/2	of Transmittal of International Search Report (20) as well as, where applicable, item 5 below.
117-321 International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
		01/10/1000
PCT/US 00/26797	29/09/2000	01/10/1999
Applicant		•
INSTITUTE OF MOLECULAR AN	D CELL BIOLOGY et al.	
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Auth ansmitted to the International Bureau.	nority and is transmitted to the applicant
This International Search Report consists  X It is also accompanied by	of a total of sheets. a copy of each prior art document cited in this	report.
Basis of the report		
a. With regard to the language, the language in which it was filed, unl	international search was carried out on the bas ess otherwise indicated under this item.	sis of the international application in the
the international search w Authority (Rule 23.1(b)).	as carried out on the basis of a translation of the	ne international application furnished to this
was carried out on the basis of the contained in the internation	e sequence listing : nal application in written form.	ternational application, the international search
filed together with the international application in computer readable form.  furnished subsequently to this Authority in written form.		
furnished subsequently to this Authority in computer readble form.		
the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.		
		s identical to the written sequence listing has been
2. X. Certain claims were four	nd unsearchable (See Box I).	
3. Unity of invention is lack	king (see Box II).	
4. With regard to the title,		
the text is approved as su	bmitted by the applicant.	
	ned by this Authority to read as follows:	
DIHYDROOROTATE DEHYDRO DISEASES	GENASE INHIBITORS FOR THE T	REATMENT OF VIRAL-MEDIATED
5. With regard to the abstract,		
X , the text is approved as sul		
the text has been establish within one month from the	ned, according to Rule 38.2(b), by this Authorit date of mailing of this international search rep	y as it appears in Box III. The applicant may, ort, submit comments to this Authority.
6. The figure of the drawings to be publi	shed with the abstract is Figure No.	
as suggested by the applic		None of the figures.
because the applicant faile		
because this figure better	characterizes the invention.	

#### INTERNATIONAL SEARCH REPORT

International Application No

A. SSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/00 A61K31/47 A61K31/4709 A61K31/497 A61K31/473
A61K31/4184 A61K31/122 A61K31/196 C07D215/52 A61P31/14
A61K38/21 A61K31/711 A61K31/343 A61K31/437 //(A61K38/21,

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7-A61K-A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, CHEM ABS Data, EMBASE, BIOSIS

	ENTS CONSIDERED TO BE RELEVANT	· · · · · · · · · · · · · · · · · · ·
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 680 299 A (HESSON DAVID P) 14 July 1987 (1987-07-14) cited in the application examples 28,197,198; tables 1,6	2-14, 26-28
<b>A</b>	EP 0 601 191 A (KYOWA HAKKO KOGYO KK) 15 June 1994 (1994-06-15) page 3, line 8-30 page 12, line 40-55; claims 1-3	2-14, 26-28
Α	PATENT ABSTRACTS OF JAPAN vol. 1998, no. 14, 31 December 1998 (1998-12-31) & JP 10 231289 A (KYOWA HAKKO KOGYO CO LTD), 2 September 1998 (1998-09-02) cited in the application abstract	2-14, 26-28

	-/
Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents:  'A' document defining the general state of the art which is not considered to be of particular relevance  'E' earlier document but published on or after the international filing date  'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  'O' document referring to an oral disclosure, use, exhibition or other means  'P' document published prior to the international filing date but later than the priority date claimed	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> <li>"3" document member of the same patent family</li> </ul>
Date of the actual completion of the international search	Date of mailing of the international search report
14 December 2001	02/01/2002
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040. Tx. 31 651 epo nl.  Fax: (+31-70) 340-3016	Authorized officer  Kling, I

### INTERNATIONAL SEARCH REPORT

l	Internationa	Application No
l	US	00/26797

IPC 7	31:00), (A61K31/711,31:00), (A61K3	1/437,31:00),(A61K31/34	3,31:00)
	Classification (IDC) and half actional description		
	to International Patent Classification (IPC) or to both national classi	rication and IPC	
	documentation searched (classification system followed by classific	ation symbols)	
Documenta	ation searched other than minimum documentation to the extent tha	it such documents are included in the fields s	earched
Electronic o	data base consulted during the international search (name of data	base and, where practical, search terms used	<b>d</b> )
		·	
	•		
C DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the r	relevant nassages	Relevant to claim No.
	Challer of Good and the Challer of t		
A	EP 0 721 942 A (KYOWA HAKKO KOGY 17 July 1996 (1996-07-17) claims 1-5; examples 11-46	'0 KK)	2-14, 26-28
		·	*
	·		•
	ner documents are listed in the continuation of box C.	Patent family members are listed	n annex.
	tegories of cited documents :	'T' later document published after the inter- or priority date and not in conflict with it	national filing date
	ent defining the general state of the art which is not ered to be of particular relevance	cited to understand the principle or the invention	
"E" earlier d	tocument but published on or after the international ate	"X" document of particular relevance; the cl cannot be considered novel or cannot	aimed invention
"L" docume	nt which may throw doubts on priority daim(s) or is cited to establish the publication date of another	involve an inventive step when the doc	ument is taken alone
citation	or other special reason (as specified)	"Y" document of particular relevance; the cl cannot be considered to involve an inv document is combined with one or more	entive step when the
other n		ments, such combination being obviou in the art.	s to a person skilled
	nt published prior to the international filing date but an the priority date claimed	*&* document member of the same patent f.	amily
Date of the a	actual completion of the international search	Date of mailing of the international sea	ch report
14	4 December 2001		
Name and m	nailing address of the ISA	Authorized officer	
	European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk		
	Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Kling, I	Ī

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1, 15-25, 29-34

Present claims 1, 15-25, 29 -34 relate to a use and respectively to a product and to a method defined by reference to a desirable characteristic or property, namely to an "inhibitor of dihydroorotate dehydrogenase"

The claims cover all uses, products, methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the use, product and method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use or the product containing the compounds of formula (I), (Ia), (II), (IIb), (I') (III), (IV), (V), (VI), (VII) (VIII) and the compounds of formula (IIa) e.g those prepared in examples 1 to 3 and mentioned in Tables 1 to 3

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Box i	Observations where certain claims were found unsearchable (Continuation of item 1 of first sh et)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X	Furthermore, claims 29 and 30 are directed to a method of treatment of the human/animal body, the search has not been carried out and based on the alleged effects of the compound/composition, since these claims are not clear according to art. 6 PCT.  Claims Nos.:  1, 15-25, 29-34  because they relate to parts of the Internal Application that do not comply with the prescribed requirements to such
	an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inter	rnational Searching Authority found multiple inventions in this international application, as follows:
	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4 n	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is estricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark o	n Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.

### INTERNATIONAL SEARCH REPORT

nt tion on patent family members

International Application No
/US 00/26797

						<del></del>
	Patent decument- ed in search report		Patilication		Patent/amily: member(s)	date
US	4680299	A	14-07-1987	US AT AU AU	5032597 A 58834 T 583793 B2 3085284 A	16-07-1991 15-12-1990 11-05-1989 24-01-1985
			,	CA DE DK EP ES	1288436 A1 3483704 D1 358784 A 0133244 A2 534509 D0	03-09-1991 17-01-1991 23-01-1985 20-02-1985 01-09-1985
				ES FI GR	8507498 A1 842928 A ,B, 82234 A1	16-12-1985 23-01-1985 13-12-1984 15-09-1995
				HK HU IE IL LV	142395 A 35248 A2 57627 B1 72471 A 5701 A3	28-06-1985 10-02-1993 15-11-1988 20-02-1995
				MX NO NZ PT SG	158610 A 842969 A ,B, 208966 A 78960 A ,B 128393 G	20-02-1989 23-01-1985 05-12-1986 01-08-1984 25-02-1994
				SU SU	1393314 A3 1452480 A3	30-04-1988 15-01-1989
EP	0601191	Α	15-06-1994	DE DE DK	69319859 D1 69319859 T2 601191 T3	27-08-1998 17-12-1998 26-04-1999
				EP JP US AT	0601191 A1 2928385 B2 5371225 A 168679 T	15-06-1994 03-08-1999 06-12-1994 15-08-1998
				CA ES WO	2111955 A1 2120498 T3 9322286 A1	11-11-1993 01-11-1998 11-11-1993
JP	10231289	А	02-09-1998	NONE		
EP	0721942	Α	17-07-1996	AU EP US CA WO	7707094 A 0721942 A1 5646283 A 2150235 A1 9509153 A1	18-04-1995 17-07-1996 08-07-1997 06-04-1995 06-04-1995